Set Name side by side	**Query**	**Hit Count**	**Set Name** result set
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L17	L16 with l15 with l14 with l6	27	L17
L16	l1 or l4	1417861	L16
L15	AQUEOUS	875317	L15
L14	alcohol or PVA	653344	L14
L13	L12 with l6	3	L13
L12	l4 with l3	53	L12
L11	L10 with l5	16	L11
L10	L8 with l3	3445	L10
L9	L8 and l3	8041	L9
L8	L7 or l1	1452645	L8
L7	peg	68146	L7
L6	dna or plasmid or nucleic or polynucleotide	181920	L6
L5	dna or plasmid or nucleic	175535	L5
L4	microparticle or microsphere	33241	L4
L3	negatively charged lipid or DPSE or DOPE	40676	L3
L2	s negatively charged lipid or DPSE or DOPE	40411	L2
L1	s peg or polymer	1403779	L1

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Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L17

Refine Search

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Search History

DATE: Tuesday, January 14, 2003 Printable Copy Create Case

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L17: Entry 2 of 27 File: PGPB Jun 27, 2002

DOCUMENT-IDENTIFIER: US 20020082237 A1
TITLE: Cationic polymers and lipids for the delivery of nucleic acids

Summary of Invention Paragraph (29):
[0024] Another embodiment of the present invention includes a novel process for making polynucleotide delivery vehicles comprising the steps of complexing the polynucleotide and cationic polymer and/or cationic lipid in buffer that maintains DNA as a B-form helix (e.g., an aqueous alcohol solution), and removing the buffer by evaporation. After reconstitution of the dried polynucleotide-cationic lipid/cationic polymer complex with aqueous solution, stable polynucleotide delivery vehicles are produce.

```
     (FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS, BIOTECHDS' ENTERED AT 14:03:35
     ON 14 JAN 2003)
                DEL HIS
L23       873716 S POLYME? OR MICROPARTICLE OR MICROSPHERE
L24       536386 S LIPID OR AMPHIPHILE
L25         9979 S L24 AND L23
L26      2369734 S DNA OR NUCLEIC OR PLASMID
L27         2961 S L26 AND L25
L28        30437 S PEG
L29           33 S L28 AND L27
L30           14 DUP REM L29 (19 DUPLICATES REMOVED)
L31         1987 S PLG
L32            5 S L31 AND  L27
L33            2 DUP REM L32 (3 DUPLICATES REMOVED)
L34      4660255 S MICRO?
L35          758 S L34 AND L27
L36          552 DUP REM L35 (206 DUPLICATES REMOVED)
L37        35164 S ANIONIC OR NEGATIVELY CHARGED LIPID
L38         3822 S L37 AND L24
L39          413 S DSPE
L40           10 S L39 AND L38
L41            5 DUP REM L40 (5 DUPLICATES REMOVED)
L42           53 S L39 AND L25
L43           27 DUP REM L42 (26 DUPLICATES REMOVED)
L44           40 SS L27 AND (L37 OR L39)
L45           23 DUP REM L44 (17 DUPLICATES REMOVED)
L46         2932 S MICROPARTICLE
L47           16 S L46 AND L27
L48           11 DUP REM L47 (5 DUPLICATES REMOVED)
```

PALM INTRANET

Day : Tuesday
Date: 1/14/2003
Time: 15:46:41

Continuity Information for 09/909460

Parent Data

09909460
is a continuation of 09321346
Which is a continuation in part of 09266463
Which is a continuation in part of 09003253
Which Claims Priority from Provisional Application 60035983
Which is a continuation in part of **PCT/US98/01499** International Filing Date: **01/22/1998**

Child Data

No Child Data

Appln Info | Contents | Petition Info | Atty/Agent Info | **Continuity Data** | Foreign Data | Inventors

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PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search

Attorney Docket # [ ] Search

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L30 ANSWER 12 OF 14 MEDLINE DUPLICATE 8
AN 1999337493 MEDLINE
DN 99337493 PubMed ID: 10407066
TI Stabilized **plasmid-lipid** particles: factors influencing **plasmid** entrapment and transfection properties.
AU Mok K W; Lam A M; Cullis P R
CS Department of Biochemistry and Molecular Biology, University of British Columbia, 2146 Health Sciences Mall, Vancouver, B.C. V6T 1Z3, Canada.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Jul 15) 1419 (2) 137-50.
Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990903
AB Previous work has shown that **plasmid DNA** can be encapsulated in small 'stabilized **plasmid-lipid** particles' (SPLP) composed of 1, 2-dioleyl-3-phosphatidylethanolamine (DOPE), the cationic **lipid** N, N-dioleyl-N,N-dimethylammonium chloride (DODAC) and poly(ethylene glycol) (**PEG**) conjugated ceramides (**PEG**-Cer), employing a detergent dialysis procedure. These SPLP have potential as vectors for in vivo gene therapy. This study is aimed at characterizing the influence of the cationic **lipid** and **PEG**-Cer species on SPLP formation and in vitro transfection properties. It is shown that the transfection potency of SPLP is sensitive to the cationic **lipid** species employed, the size of the **PEG polymer** incorporated in the **PEG**-ceramide and the length of the acyl chain contained in the ceramide anchor. With regard to the influence of cationic **lipid**, the transfection levels achieved were highest for SPLP containing N-[2, 3-(dioleyloxy)propyl]-N,N-dimethyl-N-cyanomethylammonium chloride (DODMA-AN) and lowest for SPLP containing 3-beta-[N-(N', N'-dimethylaminoethyl)carbamoyl]-cholesterol (DC-CHOL), according to the series DODMA-AN>N-[2,3-(dioleyloxy)propyl]-N,N, N-trimethylammonium chloride (DOTMA)>DODAC>N,N-distearyl-N, N-dimethylammonium chloride (DSDAC)>DC-CHOL. Incorporation of short (**PEG**(750)) **PEG polymers** in the **PEG**-ceramide components resulted in modest improvements in transfection levels over **PEG**(2000) and **PEG**(5000) **polymers**, however variation of the length of the acyl chain contained in the hydrophobic ceramide anchor from octanoyl (**PEG**-CerC(8)) to myristoyl (**PEG**-CerC(14)) to arachidoyl (**PEG**-CerC(20)) had the most dramatic effects. Transfection levels achieved for SPLP containing **PEG**-CerC(8) were substantially larger than observed for SPLP containing **PEG**-CerC(14) or **PEG**-CerC(20), consistent with a requirement for the **PEG**-ceramide to dissociate from the SPLP surface for maximum transfection potency. It is also shown that the ability of SPLP to be accumulated into cells is a dominant factor influencing transfection potency, and that the transfection potency of SPLP that are accumulated is at least equivalent to that of cationic **lipid-plasmid DNA** complexes.

L30 ANSWER 11 OF 14 MEDLINE DUPLICATE 7
AN 1999363970 MEDLINE
DN 99363970 PubMed ID: 10435112
TI Stabilized **plasmid-lipid** particles: construction and characterization.
AU Wheeler J J; Palmer L; Ossanlou M; MacLachlan I; Graham R W; Zhang Y P; Hope M J; Scherrer P; Cullis P R
CS Inex Pharmaceuticals Corporation, Burnaby, BC, Canada.
SO GENE THERAPY, (1999 Feb) 6 (2) 271-81.
Journal code: 9421525. ISSN: 0969-7128.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990817
AB A detergent dialysis procedure is described which allows encapsulation of **plasmid DNA** within a **lipid** envelope, where the resulting particle is stabilized in aqueous media by the presence of a poly(ethyleneglycol) (**PEG**) coating. These 'stabilized **plasmid-lipid** particles' (SPLP) exhibit an average size of 70 nm in diameter, contain one **plasmid** per particle and fully protect the encapsulated **plasmid** from digestion by serum nucleases and E. coli DNase I. Encapsulation is a sensitive function of cationic **lipid** content, with maximum entrapment observed at dioleoyldimethylammonium chloride (DODAC) contents of 5 to 10 mol%. The formulation process results in **plasmid**-trapping efficiencies of up to 70% and permits inclusion of 'fusigenic' lipids such as dioleoylphosphatidylethanolamine (DOPE). The in vitro transfection capabilities of SPLP are demonstrated to be strongly dependent on the length of the acyl chain contained in the ceramide group used to anchor the **PEG polymer** to the surface of the SPLP. Shorter acyl chain lengths result in a **PEG** coating which can dissociate from the SPLP surface, transforming the SPLP from a stable particle to a transfection-competent entity. It is suggested that SPLP may have utility as systemic gene delivery systems for gene therapy protocols.

L30 ANSWER 2 OF 14 MEDLINE DUPLICATE 1
AN 2002200333 MEDLINE
DN 21848587 PubMed ID: 11858858
TI Protective immune responses elicited in mice by immunization with formulations of poly(lactide-co-glycolide) microparticles.
AU McKeever U; Barman S; Hao T; Chambers P; Song S; Lunsford L; Hsu Y-Y; Roy K; Hedley M L
CS Zycos Inc., 44 Hartwell Avenue, Lexington, MA 02421, USA.
SO VACCINE, (2002 Feb 22) 20 (11-12) 1524-31.
Journal code: 8406899. ISSN: 0264-410X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200209
ED Entered STN: 20020406
Last Updated on STN: 20020928
Entered Medline: 20020927
AB Parenteral administration of **microparticle** encapsulated **DNA** elicits immune responses to the encoded antigens. Experiments were performed to test whether the addition of certain lipophilic agents to such formulations enhanced the activity of a beta-galactosidase (beta-gal) **DNA** vaccine. Addition of either taurocholic acid (TA) or monomethoxy polyethylene-glycol-distearoylphosphatidylehanolamine (**PEG**-DSPE) increased the efficiency of **DNA** encapsulation. Immunization of mice with encapsulated **DNA** formulations containing either compound significantly increased the number of antibody positive responders over that achieved with non-**lipid** containing particles. Moreover, responding animals demonstrated trends towards higher antibody titers and increased T cell responses. Tumor protection against the CT26.CL25 tumor cell line was demonstrated with **lipid** and non-**lipid** containing formulations. These results are the first demonstration of protection obtained by parenteral administration of PLG encapsulated **DNA** vaccines.

L33 ANSWER 1 OF 2 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2002-11585 BIOTECHDS
TI Novel **nucleic** acid delivery system useful for preparation of composition for delivering **nucleic** acid to subject and for treating/preventing cancer, comprises **DNA** encapsulated in biodegradable **polymeric** microspheres;
recombinant vector-mediated gene transfer and expression in host cell for use in recombinant vaccine and **nucleic** acid vaccine preparation and cancer prevention, therapy and gene therapy
AU JOHNSON M E; MOSSMAN S; CECIL T; EVANS L
PA CORIXA CORP
PI WO 2002003961 17 Jan 2002
AI WO 2000-US21780 7 Jul 2000
PRAI US 2000-216604 7 Jul 2000
DT Patent
LA English
OS WPI: 2002-257248 [30]
AB DERWENT ABSTRACT:
NOVELTY - A **nucleic** acid delivery system (I) comprising deoxyribonucleic acid (**DNA**) encapsulated in biodegradable **polymeric** microspheres, where at least 50% of the **DNA** comprises supercoiled **DNA**, and where at least 50% of the **DNA** is released from the microspheres after 7 days at about 37 degrees C, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) encapsulating (M) **nucleic** acid molecules in microspheres by dissolving a **polymer** in a solvent to form a **polymer** solution, adding an aqueous solution containing **nucleic** acid molecules to the **polymer** solution to form a primary emulsion, homogenizing the primary emulsion, mixing the primary emulsion with a process medium comprising a stabilizer to form a secondary emulsion, and extracting the solvent from the secondary emulsion to form microspheres encapsulating **nucleic** acid molecules; (2) a pharmaceutical composition (II) comprising **nucleic** acid molecules encapsulated in microspheres produced by (M); and (3) use of an aminoalkyl glucosaminide 4-phosphate (AGP) (III) for the preparation of an adjuvant for enhancing the immunostimulatory efficacy of microspheres encapsulating **nucleic** acid molecules.

WIDER DISCLOSURE - Also disclosed is an adjuvant for modulating the immunostimulatory efficacy of microspheres encapsulating **nucleic** acid molecules comprising aminoalkyl glucosaminide 4-phosphate (AGP).

BIOTECHNOLOGY - Preferred System: In (I), the microspheres have an encapsulation efficiency of at least about 40%. At least about 70% of the **DNA** is released from the microspheres after 7 days at about 37 degrees C. At least about 90% of the microspheres are about 1-10 microm in diameter. The microspheres comprise poly(lacto-co-glycolide) (**PLG**). (I) further comprises an adjuvant comprising AGP. The **DNA** encodes an antigen such as her2/neu associated with cancer, preferably breast cancer or an antigen such as TbH9 associated with infectious disease, preferably tuberculosis. Preferred Method: In (M), the **polymer** comprises **PLG** including ester end groups or carboxylic acid end groups. The **PLG** has a molecular weight of from about 8-65 kDa. The **nucleic** acid molecules are maintained at about 2-35 degrees C, preferably 4-25 degrees C prior to the extraction. The solvent comprises dichloromethane, chloroform, or ethylacetate. The **polymer** solution further comprises a cationic **lipid**, and an adjuvant comprising MPL. The stabilizer comprises carboxymethylcellulose (CMC), polyvinyl alcohol (PVA), or a mixture of CMC and PVA, and a cationic **lipid**. The stabilizer comprises from about 1-5% of the process medium. The solvent comprises an internal water volume of from about 0.001-0.5%. The aqueous solution comprises an

ethanol content of from about 0-75% (v/v). The **nucleic** acid molecule comprises **DNA**. The aqueous solution comprises about 0.2-12 mg/ml **DNA** comprising a **plasmid** of about 3-9 kb. The aqueous solution further comprises an adjuvant such as QS21, and a stabilizer comprising bovine serum albumin. At least 50% of the **DNA** retains a supercoiled formation through the extraction step. The encapsulation efficiency is at least about 40%. The microspheres release at least about 50% of the **nucleic** acid molecules within about 7 days, preferably 4 days. Preferred Composition: (II) further comprises an adjuvant such as AGP. Preferred Adjuvant: (III) comprises an aqueous formulation. (III) is preferably 517, 527, 547, 557 or 568. (III) is administered simultaneously with the microspheres, or before or after administration of the microspheres.

ACTIVITY - Cytostatic; tuberculostatic.

MECHANISM OF ACTION - Enhancer of immunostimulatory efficacy of microspheres encapsulating **nucleic** acid molecules (claimed); vaccine; gene therapy. Immune responses elicited in monkeys by encapsulated **DNA** was tested: The immune responses elicited in rhesus macaques following three immunizations, at monthly intervals, with either naked TbH9-VR1012 **DNA** or TbH9-VR1012 **DNA** encapsulated in microspheres were tested. Naked **DNA** consisted of 3.3 mg **plasmid** + 40 microg RC527-AF, immunized by intradermal and intramuscular routes. Microspheres **DNA** consisted of 3 mg **plasmid** + 50 microg RC 568-Af delivered intramuscularly. There were four animals in each group. The results, demonstrated that the **microsphere**-encapsulated **DNA** elicited stronger immune responses than were observed with naked **DNA**.

USE - (I) is useful for the preparation of a composition for delivering a **nucleic** acid molecule to a subject, for eliciting an immune response to an antigen in a subject, for treating or preventing a cancer associated with her2/neu antigen or tuberculosis in a subject. (III) is useful for the preparation of an adjuvant for enhancing the immunostimulatory efficacy of microspheres encapsulating **nucleic** acid molecules (claimed). (I) is useful for delivery of vaccines, preferably **DNA** vaccines.

ADMINISTRATION - (II) is administered by parenteral (e.g., intravenous, subcutaneous, intramuscular), buccal, sublingual, rectal, oral, nasal, topical (e.g., transdermal, ophthalmic), vaginal, pulmonary, intraarterial, intraperitoneal, intraocular, or intranasal route or directly into a specific tissue. No dosage details are given.

ADVANTAGE - (I) offers, in one system, a combination of high encapsulation efficiency, rapid release kinetics and preservation of **DNA** in supercoiled form.

EXAMPLE - The formulation of a **DNA** poly(lacto-co-glycolide) (**PLG**) microspheres with desirable in vitro characteristics was as follows. Specifically, 1-10 microm diameter microspheres which were able to release their **DNA** contents over the course of a week were prepared using a process that resulted in a high encapsulation efficiency (60-80%) and high rate of retention of the **DNA** supercoiled state (70%). **PLG** microspheres containing **DNA** encoding antigenic proteins were prepared using variations on the double emulsion technique (J.H. Eldridge et al. Mol Immunol, 28:287-294, 1991; S. Cohen et al. Pharm Res, 8:713-720, 1991)). Specifically, **plasmid DNA** in Tris-ethylenediaminetetraacetic acid (EDTA) buffer, 0.38 ml ethanol were combined and brought up to a volume of 5.1 ml using Tris-EDTA buffer. This was the internal (water) phase. 1200 mg of **PLG** **polymer** was dissolved in 13.9 ml of dichloromethane (DCM) and put on ice. The internal aqueous phase was added to the **PLG** solution and mixed in a 30 ml syringe while still on ice using a Polytron tissue homogenizer for 20 seconds to form the primary emulsion

(water-in-oil). The secondary emulsion was prepared by adding the primary emulsion to a beaker containing 280 ml of 1.4% carboxymethylcellulose), or process medium, on ice, and mixing. The secondary emulsion was diluted with miliQ water, and mixed in order to extract dichloromethane from, and to harden, the microspheres. The resulting microspheres were washed and centrifuged. After washing, mannitol was added to the concentrated microspheres, which were frozen and lyophilized. Lyophilized microspheres were then assayed for their size distribution, **DNA** content, release kinetics, and the supercoiled content of the encapsulated **DNA**. Two plasmids were used in this study, one encoding a tuberculosis antigen, TbH9, and the other encoding the breast cancer antigen, Her-2/neu. Mice were immunized with **DNA** microspheres dispersed in aqueous buffer. The combination of microspheres with selected aminoalkyl glucosaminide 4-phosphate (AGP) was investigated by using a sub-optimal immunization schedule, a single 10 microg dose of encapsulated **DNA** dispersed in phosphate buffer saline (PBS) along with 10 microg of adjuvant. Lastly, the effect of the resuspension buffer was examined by administering to mice a single 10 microg dose of encapsulated **DNA** dispersed in either PBS or sodium chloride free phosphate buffer (PB). The process resulted in microspheres that were small (about 1-10 microm in diameter), with rapid release kinetics, high encapsulation efficiency (40-80%), and good retention of supercoiled **DNA**. More than 33% of the **microsphere** contents were released after 48 hours in vitro at 37 degrees C, more than 50% were released after 4 days, and more than 70% after 7 days. The ratio of supercoiled-to-nicked **DNA** for the **plasmid** extracted from the microspheres was more than 50% of the ratio of the input **DNA**. (60 pages)

L41 ANSWER 5 OF 5 MEDLINE DUPLICATE 3
AN 2000419156 MEDLINE
DN 20302306 PubMed ID: 10845683
TI Novel therapeutic nano-particles (lipocores): trapping poorly water soluble compounds.
AU Perkins W R; Ahmad I; Li X; Hirsh D J; Masters G R; Fecko C J; Lee J; Ali S; Nguyen J; Schupsky J; Herbert C; Janoff A S; Mayhew E
CS The Liposome Company, Inc., Princeton, NJ 08540, USA.. wperkins@lipo.com
SO INTERNATIONAL JOURNAL OF PHARMACEUTICS, (2000 Apr 25) 200 (1) 27-39. Journal code: 7804127. ISSN: 0378-5173.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000901
AB The development of stable spherical **lipid**-coated drug particles that are termed 'lipocores' is reported here. Unlike conventional **lipid**-based particles (i.e. liposomes, emulsions, micelles), these particles are comprised solely of a core of a poorly water soluble drug surrounded by polyethyleneglycol conjugated **lipid** (PEG-**lipid**) and are formed via a 'kinetic' trapping process. These lipocore particles were made with the acyl chain of 16 carbon length (C16) acyl-chain derivatives of paclitaxel or vinblastine and with the polyene antifungal hamycin. Formation of the particles occurred regardless of the type of PEG-phospholipid used (i.e. acyl chain length, chain saturation, and polymer length) and could also be formed with the **negatively charged lipid** N-glutaryl-dioleoyl-phosphatidylethanolamine (DOPE-GA). Images from both freeze-fracture electron microscopy and electron cryo-microscopy revealed solid spherical structures with no internal lamellae for the PEG-**lipid** particles made with the C16 derivatives of paclitaxel (BrC16-T) or vinblastine (C16-Vin). From a solute distribution study of lipocores made with BrC16-T and distearoyl-phosphatidylethanolamine-PEG2000 (**DSPE**-PEG2000), the particles were found to have no measurable aqueous captured volume. Fluorescence anisotropy and order parameter measurements revealed the core material of these particles to be highly immobilized. The mole ratio of BrC16-T:**lipid** in the lipocores was typically > 90: < 10 and as high as 98:2, and the refrigerated lipocores were stable for several months. BrC16-T/**DSPE**-PEG2000 lipocores of 50-100 nm particle size were far less toxic than paclitaxel (Taxol) after intraperitoneally (i.p.) or intravenously (i.v.) administration in mice and were active against i.p. and subcutaneously (s.c.) planted human (OvCar3) ovarian carcinoma grown in SCID mice. It is believed the high drug:**lipid** ratio, the stability, and therapeutic efficacy of these novel particles make them a paradigm for delivery of poorly water soluble drugs and/or their hydrophobic derivatives.

L41 ANSWER 2 OF 5 MEDLINE
AN 2003013680 IN-PROCESS
DN 22407987 PubMed ID: 12519628
TI THE TRANSFECTION OF JURKAT T-LEUKEMIC CELLS BY USE OF pH-SENSITIVE IMMUNOLIPOSOMES.
AU Turner Christopher; Weir Neil; Catterall Catherine; Baker Terry S; Carrington Bruce; Jones Malcolm N
CS Liposome Research Unit, University of British Columbia, Vancouver, BC, V6T 123, Canada.
SO J Liposome Res, (2002 Nov) 12 (4) 311-34.
Journal code: 9001952. ISSN: 0898-2104.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030110
Last Updated on STN: 20030110
AB A gene transfer vector has been developed utilising **anionic** liposomes as a carrier of plasmid DNA (pEGlacZ, 7.6 kb) to transfect CD3+ T lymphocytes (Jurkat cells). The plasmid DNA that contained the Escherichia coli beta-galactosidase reporter gene was condensed using poly-l-lysine of molecular mass 20,700 (PLK99) to form a polyplex which was interacted with several **anionic** liposome formulations to form lipopolyplexes. The liposome formulations where based on dioleoylphosphatidylethanolamine (DOPE) in combination with cholesterol and dioleoylphosphatidylcholine (DOPC) and oleic acid, or dimyristoylphosphatidylethanolamine (DMPE). For targeting to the Jurkat cells distearoylphosphatidylethanolamine (**DSPE**) linked to poly (ethylene glycol) molecular mass 2000 and coupled to anti-CD3 antibody was incorporated. The polyplexes and lipopolyplexes were characterised in terms of size, zeta potential, agarose gel electrophoresis and electron microscopy and the permeability of the lipopolyplexes to liposome-encapsulated glucose was determined. The polyplexes consisted of a mixed population of rod-like structures (53-160 nm long and 23-31 nm diameter) and spheres (18-30 nm diameter). The lipopolyplexes retained a permeability barrier although were more permeable to glucose than their component liposomes. The poly-l-lysine condensing agent was still susceptible to pronase digestion suggesting that the polyplex was associated with the outer surface of the liposome. The lipopolyplexes with **lipid** composition DOPE/cholesterol/OA/**DSPE**-PEG2000 anti-CD3+ PLK99-plasmid DNA had significant gene transfer activity, as monitored by beta-galactosidase expression, that depended on the charge ratio of the component polyplex and the **lipid**/DNA weight ratio. The anti-CD3 antibody, the liposomal **lipid** and pH sensitivity were essential for transfection activity.

L43 ANSWER 27 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 93131099 EMBASE
DN 1993131099
TI Rationale for the control of the biological properties of **lipid** membranes in vitro and in vivo.
AU Cevc G.; Blume G.
CS Medizinische Biophysik, Urologische Klinik und Poliklinik, Technische Universitat, Ismaningerstr. 22,D-8000 Munchen 8, Germany
SO Acta Pharmaceutica, (1992) 42/4 (263-271).
ISSN: 1330-0075 CODEN: ACPHEE
CY Croatia
DT Journal; Conference Article
FS 029 Clinical Biochemistry
LA English
SL English; Slovenian
AB **Lipid** membranes are being used increasingly in many biotechnological and biological systems. For the success of such applications it is crucial to understand and quantify the interactions between **lipid** bilayers and soluble macromolecules, however. We argue that the efficiency of specific binding of any large molecule (e.g. an antibody) to its ligand attached to a **lipid** membrane is diminished by the proximity of the bilayer surface. This appears to be due to the same non-Coulombic, hydration dependent short-range force which also prevents the colloidal collapse of a stack of **lipid** membranes. The strength of this force, as a rule, decreases with decreasing polarity of the **lipid** headgroups. Nonspecific protein adsorption of the **lipid** bilayers, on the contrary, is little affected by the overall repulsion between a macromolecule and the bilayer surface; rather, this adsorption is governed by the number of defects and/or by the available hydrophobic binding sites in a given membrane. Multiple nonspecific protein adsorption, which results in the macromolecular denaturation, is one of the main reasons for the rapid elimination of **lipid** vesicles from the blood stream in vivo. To promote the longevity of liposomes it is therefore necessary to modify the surfaces of their constituent **lipid** bilayers. Increasing the surface density of the net charges and/or the bilayer surface hydrophilicity is of little use in this respect; to affect the nonspecific bilayer-protein interactions singificantly, an optimal number of water soluble, short **polymers** should be attached to the **lipid** headgroups. These increase the repulsive barrier of the **lipid** membrane surface and often may prolong the life-time of the resulting **lipid** vesicles dramatically. Vesicles consisting of a 8/2 (mol mol-1) mixture of distearoylphosphatidylethanolamine-PEG (**DSPE** -PEG) with distearoylphosphatidylcholine or of a 7/3 (mol mol-1) mixture **DSPE**-PEG and soy-bean phosphatidylcholine, for example, remain in the murine circulation 8 to 10 times longer than standard phosphatidylcholine liposomes. The **polymer**-coated long-lived liposomes, moreover, have a lower affinity for protein binding, induce less protein denaturation, are not very attractive to phagocytic cells, and also accumulate highly efficiently in tumors.

L43 ANSWER 23 OF 27 MEDLINE
AN 95178599 MEDLINE
DN 95178599 PubMed ID: 7873652
TI New amphipatic **polymer-lipid** conjugates forming
long-circulating reticuloendothelial system-evading liposomes.
AU Woodle M C; Engbers C M; Zalipsky S
CS Liposome Technology, Inc., Menlo Park, California 94025.
SO BIOCONJUGATE CHEMISTRY, (1994 Nov-Dec) 5 (6) 493-6.
Journal code: 9010319. ISSN: 1043-1802.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950419
Last Updated on STN: 19950419
Entered Medline: 19950404
AB **Lipid**-conjugates of two amphipatic **polymers**,
poly(2-methyl-2-oxazoline) (PMOZ) and poly(2-ethyl-2-oxazoline) (PEOZ)
(degree of **polymerization** approximately 50) were synthesized by
linking glutarate esters of the **polymers** to
distearoylphosphatidylethanolamine (**DSPE**) or alternatively by
termination of the **polymerization** process with **DSPE**.
Surface-modified liposomes (90 +/- 5 nm) prepared from either conjugate (5
mol % of total **lipid**) were injected into rats and followed by
blood level and tissue distribution measurements. Both **polymers**
PEOZ and PMOZ were found to convey long circulation and low hepatosplenic
uptake to liposomes to the same extent as polyethylene glycol (PEG), the
best known material for this purpose. This is the first demonstration of
protection from rapid recognition and clearance conveyed by alternative
polymers, which is equal to the effect of PEG.

L45 ANSWER 16 OF 23 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 1999-00209 BIOTECHDS
TI Processes for drug delivery, therapeutic imaging, and diagnostic imaging; used for targeted drug delivery and gene therapy
AU Unger E C
PA Imarx-Pharm.
LO Tucson, AZ, USA.
PI WO 9842383 1 Oct 1998
AI WO 1998-US3632 25 Feb 1998
PRAI US 1997-925353 8 Sep 1997; US 1997-823791 21 Mar 1997
DT Patent
LA English
OS WPI: 1998-557028 [47]
AB A method for delivering a bioactive agent (BA) to a patient is claimed, involving administration of a composition containing an **anionic lipid**, a cationic counter ion, a **lipid** covalently bonded to a **polymer**, and the BA. Therapeutic ultrasound is then applied to facilitate delivery of the BA in a desired region. An alternate method involves administering a compound containing a charged **lipid** in place of the **anionic lipid**, a counter ion in place of the cationic counter ion, and an additional targeting ligand. Also claimed is a means of providing an image of an internal region of a patient by administering the alternate compound and scanning the patient using diagnostic imaging to produce visible images of the desired region. The claims also cover a contrasting agent, composed of the constituents of the alternate composition. These compositions and processes are for use in the targeted delivery of drugs, with improved efficacy and reduced toxicity. The preferred BA is a diagnostic agent, or genetic material, e.g. recombinant **nucleic** acid, antisense **nucleic** acid, hammerhead RNA, ribozyme, hammerhead ribozyme, oligonucleotide, etc. (167pp)

L48 ANSWER 9 OF 11 MEDLINE DUPLICATE 2
AN 2001206621 MEDLINE
DN 21144495 PubMed ID: 11249656
TI Recent developments in mucosal delivery of pDNA vaccines.
AU Barnes A G; Barnfield C; Brew R; Klavinskis L S
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SO Curr Opin Mol Ther, (2000 Feb) 2 (1) 87-93. Ref: 60
Journal code: 100891485. ISSN: 1464-8431.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010417
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AB The development of **DNA** vaccination to mucosal surfaces has continued apace over the last 2 years, with the investigation of several novel delivery vehicles. There have been advances in the understanding of the basic immunological mechanisms behind the induction of immune responses by **plasmid DNA**. The mechanistic insights are paving the way for the design of a second generation of mucosally delivered **DNA** vaccines. This article reviews the recent progress in the field of **microparticle**, cationic **lipid** and bacterial delivery systems. All these mechanisms afford some protection from environmental degradation and facilitate **DNA** uptake. These methods have been compared with respect to transfection efficiency, ability to elicit a full range of immune responses and their relative safety for in vivo applications.

L48 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2001:439332 BIOSIS

DN PREV200100439332

TI Methods of forming protein-linked lipidic microparticles, and compositions thereof.

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PI US 6210707 April 03, 2001

SO Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 3, 2001) Vol. 1245, No. 1, pp. No Pagination. e-file.
ISSN: 0098-1133.

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AB The present invention provides for **lipid:nucleic** acid complexes that have increased shelf life and high transfection activity in vivo following intravenous injection, and methods of preparing such complexes. The methods generally involve contacting a **nucleic** acid with an organic polycation to produce a condensed **nucleic** acid, and then combining the condensed **nucleic** acid with a **lipid** comprising an amphiphilic cationic **lipid** to produce the **lipid:nucleic** acid complex. This complex can be further stabilized by the addition of a hydrophilic **polymer** attached to hydrophobic side chains. The complex can also be made specific for specific cells, by incorporating a targeting moiety such as an Fab' fragment attached to a hydrophilic **polymer**. The present invention further relates to lipidic microparticles with attached proteins which have been first conjugated to linker molecules having a hydrophilic **polymer** domain and a hydrophobic domain capable of stable association with the **microparticle**, or proteins which have been engineered to contain a hydrophilic domain and a **lipid** moiety permitting stable association with the **microparticle**.